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Lynparza (*olaparib*)

An overview of Lynparza and why it is authorised in the EU

What is Lynparza and what is it used for?

Lynparza is a cancer medicine used for:

- continuing treatment after initial treatment of high-grade (fast-growing) cancers of the ovaries, fallopian tubes (which connect the ovaries to the womb), and the peritoneum (membrane lining the abdomen) in:
  - women whose cancer has come back (relapsed) after previous treatment and in whom platinum-based chemotherapy has shrunk or cleared the cancer;
  - women newly diagnosed with advanced cancer with mutations (changes) in one or both genes known as *BRCA1* and *BRCA2* who have been treated with platinum-based chemotherapy and in whom this treatment has shrunk or cleared the cancer;
  - women with advanced cancer that is HRD-positive (homologous recombination deficiency; where one of the mechanisms to repair damaged DNA does not work, which can be due to a defect in certain genes such as *BRCA1* and *BRCA2*) and in whom platinum-based chemotherapy and bevacizumab has shrunk or cleared the cancer;
- treatment of HER2-negative breast cancer (when the cancer cells do not have high levels of a protein called HER2) in patients with *BRCA1* or *BRCA2* mutations when the cancer:
  - has not spread to other parts of the body following chemotherapy given before or after surgery (early breast cancer), but there is a high risk of the cancer coming back;
  - has spread beyond the original site after treatment with certain breast cancer medicines that have stopped working or were not suitable;
- continuing treatment of pancreatic cancer in patients with mutations in *BRCA1* or *BRCA2* genes that is metastatic (has spread to other parts of the body) and has not worsened after at least 4 months of platinum-based chemotherapy;
- treatment of metastatic prostate cancer in:
  - men with mutations in *BRCA1* or *BRCA2* genes in whom medical or surgical treatment to lower testosterone levels (castration) did not work and whose cancer has worsened after treatment with other prostate cancer medicines, including a new hormonal agent;

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  - men in whom medical or surgical treatment to lower testosterone levels (castration) did not work and in whom chemotherapy is not an option;
- continuing treatment of endometrial cancer, a cancer of the lining of the womb, that is mismatch repair proficient (pMMR, meaning that the cancer cells contain certain proteins that correct mistakes when DNA in dividing cells is copied), when the cancer is advanced or has come back (recurrent). It is used in combination with durvalumab (another cancer medicine) after treatment with chemotherapy and durvalumab has been completed.

Lynparza contains the active substance olaparib. It is either used alone or in combination with other cancer medicines like bevacizumab in ovarian cancer, hormone therapy in breast cancer, abiraterone together with prednisone or prednisolone in prostate cancer and durvalumab in endometrial cancer.

How is Lynparza used?

Lynparza can only be obtained with a prescription and treatment should be started and supervised by a doctor experienced in the use of cancer medicines.

Lynparza is available as tablets which the patient takes twice a day.

The dose of Lynparza depends on what disease it is being used for. Treatment is continued for as long as the patient benefits from it and does not have unmanageable side effects. In advanced ovarian cancer, the doctor may stop treatment after 2 years if X-rays show no signs of the cancer. In early breast cancer, patients should be treated for up to 1 year. Treatment may be interrupted or stopped or the dose reduced if certain side effects develop.

For more information about using Lynparza, see the package leaflet or contact your doctor or pharmacist.

How does Lynparza work?

The active substance in Lynparza, olaparib, blocks the action of an enzyme called human poly ADP ribose polymerase (PARP), which helps to repair damaged DNA in normal and cancer cells during cell division. Cancer cells with mutations such as the *BRCA1* or *BRCA2* mutations rely more heavily on PARP to repair their DNA and continue dividing. Therefore, when PARP is blocked, the damaged DNA in cancer cells cannot be repaired and, as a result, the cancer cells die.

What benefits of Lynparza have been shown in studies?

Ovarian cancer

Studies show that Lynparza given on its own increases the time women with cancer of the ovary, fallopian tube or peritoneum live without their disease getting worse after treatment with platinum-based chemotherapy has shrunk or cleared the cancer:

- A study involving 295 patients with relapsed cancer found that those receiving Lynparza lived on average for 19.1 months without their disease getting worse compared with 5.5 months for patients receiving placebo (a dummy treatment).
- In another study involving 265 patients with relapsed cancer, those who took Lynparza lived on average for 8.4 months without their disease getting worse compared with 4.8 months for patients on placebo.

- In a third study involving 391 patients with advanced cancer who had *BRCA1* or *BRCA2* mutations, the disease did not get worse in around 74% of patients who took Lynparza for 2 years compared with 35% of patients on placebo.

When given with bevacizumab, Lynparza increases the time patients with HRD-positive cancer live without their disease getting worse after treatment with platinum-based chemotherapy and bevacizumab has shrunk or cleared the cancer. In a main study of 806 patients with advanced high-grade ovarian, fallopian tube or peritoneal cancer, patients whose cancer was HRD-positive and who took Lynparza for 22 months lived on average 37.2 months without their disease getting worse compared with 17.7 months for those receiving placebo.

Breast cancer

Lynparza was effective in a study involving 302 patients with HER2-negative breast cancer with *BRCA1* or *BRCA2* mutations whose cancer had spread. Patients treated with Lynparza lived on average 7.0 months without their disease getting worse compared with 4.2 months for patients treated with the doctor's choice of another cancer medicine.

Another study involved 1,836 patients with *BRCA1* or *BRCA2* mutations and HER2-negative breast cancer which had not spread to other parts of the body after chemotherapy treatment given before or after surgery. The study showed that Lynparza was effective at preventing the disease from coming back when given alone or together with hormone therapy. Lynparza was given to 921 patients, a placebo was given to 916 patients, and all patients were allowed to have hormone therapy. After 3 years, the disease had worsened or spread in 12% of patients treated with Lynparza compared with 20% of patients taking placebo.

Pancreatic cancer

In a study of 154 patients with *BRCA1* or *BRCA2* mutations who had metastatic pancreatic cancer that had not worsened during at least 4 months of treatment with platinum-based chemotherapy, Lynparza increased the time patients lived without their disease getting worse: those receiving Lynparza lived on average 7.4 months without their disease getting worse compared with 3.8 months for patients receiving placebo.

Prostate cancer

In a study of 387 men with metastatic castration-resistant prostate cancer whose cancer had worsened during treatment with another cancer medicine, Lynparza on its own was effective in patients with *BRCA1* or *BRCA2* mutations (160 patients overall): patients with these mutations and treated with Lynparza lived on average 9.8 months without their disease getting worse, compared with 3.0 months in those treated with the doctor's choice of another cancer medicine.

In a study of 796 men with metastatic and castration-resistant prostate cancer, Lynparza in combination with abiraterone and prednisone or prednisolone (hormone therapy) increased the time patients lived without their disease getting worse: those receiving Lynparza and hormone therapy lived on average 24.8 months without their disease getting worse, compared with 16.6 months in those treated with placebo (a dummy treatment) and hormone therapy.

Endometrial cancer

A main study consisting of two parts involved 718 patients with advanced or recurrent endometrial cancer who had not been treated before. Only the second part of the study looked at Lynparza treatment.

In the first part of the study, two groups of patients were given standard treatment (carboplatin and paclitaxel) plus durvalumab (another cancer medicine) and a third group was given standard treatment and placebo. Patients whose disease had not worsened since starting treatment were then included for maintenance treatment in the second part of the study.

In the second part of the study, the two groups of patients who first received standard treatment plus durvalumab continued treatment either on durvalumab in combination with Lynparza or durvalumab with a placebo.

Patients who continued treatment on durvalumab and placebo lived, on average, for 10.2 months before their disease got worse; in patients continuing on durvalumab and Lynparza this was 15.1 months. Supportive analyses showed a benefit of maintenance therapy with durvalumab and placebo or durvalumab with Lynparza in patients whose cancer was MMR deficient (dMMR). In patients whose cancer was MMR proficient (pMMR), a benefit was seen with durvalumab plus Lynparza but not with durvalumab and placebo.What are the risks associated with Lynparza?

For the full list of side effects and restrictions with Lynparza, see the package leaflet.

The most common side effects with Lynparza (which may affect more than 1 in 10 people) are nausea (feeling sick), tiredness, anaemia (low levels of red blood cells), vomiting, diarrhoea, decreased appetite, headache, neutropenia (low levels of neutrophils, a type of white blood cell that fights infection), dysgeusia (taste disturbances), cough, leucopenia (low levels of white blood cells), dizziness, dyspnoea (difficulty breathing) and dyspepsia (heartburn).

The most common severe side effects (which may affect more than 2 in 100 people) are anaemia, neutropenia, tiredness, leucopenia and thrombocytopenia (low levels of blood platelets).

Women must not breastfeed during treatment with Lynparza and for a month after stopping treatment.

Why is Lynparza authorised in the EU?

Generally, the outcome is poor for patients with ovarian, fallopian tube, or peritoneal cancer and for patients with HER2-negative breast cancer, pancreatic cancer with *BRCA* mutations, or castration-resistant prostate cancer with or without *BRCA* mutations whose cancer has spread. Lynparza can increase the time these patients live without their disease getting worse. In ovarian, fallopian tube or peritoneal cancer, Lynparza can also delay the need for the next cycle of platinum chemotherapy. In patients with endometrial cancer that is MMR proficient, Lynparza in combination with durvalumab has been shown to increase the time these patients live without their disease getting worse. There are uncertainties about the long-term benefits of Lynparza for endometrial cancer and the company will provide the final results of the main study in patients with endometrial cancer to address them.

The side effects with Lynparza are mostly mild or moderate and are generally manageable. The European Medicines Agency therefore decided that Lynparza's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Lynparza?

The company that markets Lynparza will carry out studies to further confirm the benefit, including long-term benefit, of the medicine in patients with ovarian cancer and endometrial cancer.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Lynparza have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Lynparza are continuously monitored. Side effects reported with Lynparza are carefully evaluated and any necessary action taken to protect patients.

Other information about Lynparza

Lynparza received a marketing authorisation valid throughout the EU on 16 December 2014.

Further information on Lynparza can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/lynparza.

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